7. (New) The method of treating a patient according to claim 6, wherein the tumor is pancreatic cancer.

8. (New) The method of treating a patient according to claim 6, wherein the tumor is colon cancer.

REMARKS

Claim 1 has been amended in order to recite the present invention with the specificity required by statute. New Claims 7 and 8 are presented in order to more specifically recite two preferred embodiments of the present invention. The subject matter of the amendment may be found in the specification as filed, *inter alia*, from page 4, line 21 to page 5, line 9, in Test Example 1 at page 32, et seq. and in Test Example 3 at page 34 et seq.. Accordingly, no new matter has been added.

Claims 1-6 are rejected under 35 U.S.C. §112, first paragraph, because the Examiner contends the specification, while being for certain generic 1,4-substituted cyclic amine derivatives, does not reasonably provide enablement for those derivatives containing all heteroaryl groups. In response, Claim 1 has been amended in order to address the Examiner's concerns.

Claims 1-6 are rejected under 35 U.S.C. §102(a) as anticipated by Kanda et al (WO 01/85716). This rejection is respectfully traversed.

Initially, since Kanda was not published until November 15, 2001, Applicants respectfully wish to point out it is not prior art herein. Still, the common Assignee have filed an application in the U.S. Patent and Trademark Office on January 12, 2000 that was accorded application No. 09/481,542, and which is a family-member equivalent of WO 01/85716.

The '542 application was allowed on July 3, 2001 and will be prior art under 35 U.S.C. §102(e). In that regard, while Kanda (and accordingly, the '542

application) discloses a compound having a piperidone structure, neither Kanda nor the '542 application discloses a compound having a piperidine structure. Accordingly, Claims 1-6 should not be rejected under §35 U.S.C. 102(e) for anticipation, and cannot be rejected for obviousness under §102(e)/§103.

The sole remaining issue, therefore, is the rejection of claim 6 under 35 U.S.C. §112, first paragraph, because the Examiner states the specification, while enabling treating pancreatic and colonic tumors, does not reasonably provide enablement for treating cancers other than solid tumors.

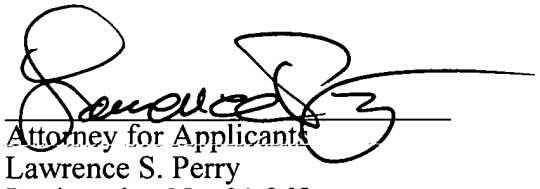
In response, Applicants demonstrated that the compounds of the present invention have activities not only on the solid tumors but also on wildly disparate tumors other than such solid tumors. A Declaration under Rule §1.132 presenting these results is attached. As readily seen from Table 1 in the Declaration, it is apparent that the compounds of the present invention have anti-tumor activities, e.g., on those very leukemia cells which have, according to the Examiner, "different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol." Accordingly, it is clear on the record those of ordinary in the art can employ Applicants' compounds without undue experimentation.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 1 to 8 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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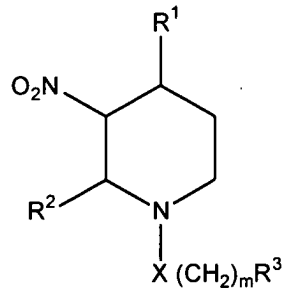
VERSION WITH MARKINGS TO SHOW CHANGES MADE TO CLAIMS

1. (Amended) A piperidine derivative represented by formula (I):



(I)

wherein

m represents an integer of 0 to 5;

R^1 and R^2 [each] independently represent a substituted or unsubstituted lower alkyl group, a substituted or unsubstituted lower alkenyl group, a substituted or unsubstituted lower alkynyl group, a substituted or unsubstituted aryl group, a substituted or unsubstituted aralkyl group, or a substituted or unsubstituted heterocyclic group;

R^3 represents a hydrogen atom, a substituted or unsubstituted alkyl group, a substituted or unsubstituted aryl group, or a substituted or unsubstituted heterocyclic group; and

X represents a bond or CO;

or a pharmaceutically acceptable salt thereof.

wherein the heterocyclic groups in R^1, R^2 and R^3 independently represent (i) a 5- or 6-membered monocyclic aromatic group containing at least one nitrogen, oxygen or sulfur atom, (ii) an aromatic group containing at least one nitrogen, oxygen or sulfur atom having two or three fused 3- to 8-membered rings, (iii) a 5- or 6-membered monocyclic or alicyclic heterocyclic group containing at least one nitrogen, oxygen or sulfur atom, or (iv) an alicyclic heterocyclic group containing at least nitrogen, oxygen or a sulfur atom having two or three fused 3- to 8-membered rings.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:	
SHINJI NARA et al.	:	Examiner: COVINGTON, ER
Serial No. 09/899,186	:	Group Art Unit: 1625
Filed: July 6, 2001	:	
For: PIPERIDINE DERIVATIVES		

DECLARATION UNDER 37 C.F.R. §1.132

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

I, Shiro Soga, a citizen of Japan, do hereby declare as follows:

I graduated from Osaka University, Faculty of Engineering Science in 1991, entered the graduate school of Osaka University immediately after graduation, and got MSc degree in 1993. My major subject in Osaka University was molecular biology. In 1993, I entered Kyowa Hakko Kogyo Co., Ltd. During 1993 and 1997, I studied on secondary metabolites of microorganisms and pharmacological effects of the metabolites on physiologically-important proteins and on animal and/or human cells at Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd. Since 1997, I have been working at Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., and studying on pharmacological effects of chemical compounds on human cells and animal. And I got PhD of Pharmacy in Tokyo University in 2002. I belong to the Japanese Molecular Biology Society. I made poster presentations in the academic meetings of this and other international societies, such as the International Conference on Dynamics and Regulation of the Stress Response, Cold Spring Harbor Laboratory Meeting on Biology of Proteolysis, and NCI-EORTC-AACR symposium on new drugs in cancer therapy. I published my work in academic journals such as Journal

of Biological Chemistry, Cancer Research, and Cancer Chemotherapy and Pharmacology.

The following experiment was conducted by me.

EXPERIMENT

Method:

On a 96-well microtiter plate (Nunc #167008), 5,000/well of leukemia (K562 or Daudi) cells were supplied, which were then pre-incubated in RPMI1640 medium containing 10% of fetal calf serum (FCS) in an incubator in the presence of 5% of a carbon dioxide gas at 37°C for 24 hours. Subsequently, a 10 mmol/L solution of the test compound in dimethylsulfoxide (DMSO) was diluted with the incubation medium and then further diluted 3-fold stepwise. The incubation was performed for additional 72 hours. After the completion of the incubation, 10 μl/well of a solution of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (Sigma, hereinafter referred to simply as MTT) in the incubation medium (final concentration: 5 mg/ml) was added to each well. After maintaining the plate at 37°C in a 5% carbon dioxide gas incubator for 4 hours, 100μl/well of 2-propanol containing 2mol/L HCl was added. After completely dissolving the MTT-formazane crystals by vigorously stirring with the use of a plate mixer, the difference in the absorbances at 550 nm and 630 nm was measured by using a microplate reader SPECTRAmax 250 (Wako Pure Chemical Industries, Ltd.) The 50% inhibitory concentration (IC_{50}) showing the proliferation inhibitory activity was calculated by using 4-parameter logistic curves of the included software SOFTmaxPRO.

Result:

Table 1: Proliferation inhibitory effect on human leukemia, K562 and Daudi, cells

Compound No.	IC_{50} (μmol/L)	
	K562	Daudi
1	11	4.4

Conclusion:

As apparent from Table 1, the present compound has an effect of inhibiting the proliferation of leukemia cells.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 may jeopardize the validity of the application or any patent issuing thereon.

Date: June 11, 2002

Shiro Soga

Shiro Soga